Transgender health 3

Global health burden and needs of transgender populations: a review

Sari L Reisner, Tonia Poteat, JoAnne Keatley, Mauro Cabral, Tampose Mothopeng, Emilia Dunham, Claire E Holland, Ryan Max, Stefan D Baral

Transgender people are a diverse population affected by a range of negative health indicators across high-income, middle-income, and low-income settings. Studies consistently document a high prevalence of adverse health outcomes in this population, including HIV and other sexually transmitted infections, mental health distress, and substance use and abuse. However, many other health areas remain understudied, population-based representative samples and longitudinal studies are few, and routine surveillance efforts for transgender population health are scarce. The absence of survey items with which to identify transgender respondents in general surveys often restricts the availability of data with which to estimate the magnitude of health inequities and characterise the population-level health of transgender people globally. Despite the limitations, there are sufficient data highlighting the unique biological, behavioural, social, and structural contextual factors surrounding health risks and resiliencies for transgender people. To mitigate these risks and foster resilience, a comprehensive approach is needed that includes gender affirmation as a public health framework, improved health systems and access to health care informed by high quality data, and effective partnerships with local transgender communities to ensure responsiveness of and cultural specificity in programming. Consideration of transgender health underscores the need to explicitly consider sex and gender pathways in epidemiological research and public health surveillance more broadly.

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This is the third in a Series of three papers about the health of transgender people

Division of General Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA (S L Reisner ScD)**; Department of Epidemiology, Harvard T H Chan School of Public Health, Boston, MA, USA** (S L Reisner)**; Fenway Institute, Fenway Health, Boston, MA, USA** (S L Reisner, E Dunham MPP)**; Department of Epidemiology** (T Poteat PhD, C E Holland MSPH, R Max MSPH, S D Baral MD) **and Department of International Health** (T Poteat)**, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Center of Excellence for Transgender Health, University**

Introduction

Transgender people are those whose assigned sex at birth differs from their current gender identity or expression, and they represent a diverse population across regions and within countries worldwide (panel 1).[1,2] Although accurate data about the size of the transgender population globally are absent and numbers depend on the definition of transgender used, estimates suggest a prevalence of 0·3–0·5% for people who identify as transgender[3] (see also paper 1 of this Series[4]). Despite their small numbers, transgender people are a population burdened by substantial adverse health indicators across high-income, middle-income, and low-income settings.[5,6] Health inequities for transgender people are hypothesised to be multifactorial, with risks including systematic social and economic marginalisation, pathologisation, stigma, discrimination, and violence, including in health-care systems and settings.[7] The purpose of the data synthesis we present here is to characterise the global health burden facing transgender populations, including the specific contexts and multiple determinants of health affecting them. We reviewed data from the peer-reviewed scientific literature to characterise the burden and distribution of disease in transgender populations globally. This synthesis of information describes transgender population health and leverages data from different regions of the world to highlight the unique sex and gender-related biological, behavioural, social, legal, and structural factors surrounding health risks and resiliencies for this underserved population. We further seek to inform future advocacy, funding, health surveillance, public health policy, monitoring, reporting processes, and research initiatives not only to address and improve health, but also to promote health equity, social justice, and human rights, including the right of all people to self-determination.

Search, selection criteria, and data synthesis

We undertook a review and synthesis of peer-reviewed recent literature (2008–14) about transgender health. We searched for "transgender" and associated terms (eg, hijra, waria, travesti, trans masculine, MTF) alongside

Key messages

- A comprehensive public health approach to address the health of transgender people requires access to gender affirmation services, evidence-based health-care delivery systems, and effective partnerships with local transgender communities
- The health-related vulnerabilities among transgender people underscore the need to explicitly consider sex and gender pathways and mechanisms in epidemiological research and public health surveillance more broadly
- Multisector partnerships linking health with advocacy, social justice, and human rights are crucial to address the public health needs of transgender people across the world
- Lack of standardised survey items on population-based surveys to identify transgender respondents limits existing public health surveillance efforts and availability of representative samples
- The global disease and health burden of transgender people remains understudied, particularly the impact of stigma, discrimination, violence, and other social and structural factors that affect the health of this underserved population, as well as interventions to mitigate stigma
- Despite substantial gaps in empirical research, there are sufficient actionable data highlighting unique biological, behavioural, social, and structural contextual factors surrounding health risks and resiliencies for transgender people that need interventions
- Consistency of definitions for health surveillance and research initiatives that include transgender people are essential, including dedicated funding to support these efforts

of California San Francisco, San Francisco, CA, USA (J Keatley MSW); Global Action for Trans* Equality, Buenos Aires, Argentina and New York, NY, USA (M Cabral); MATRIX, Lesotho, Africa (T Mothopeng); and Heller School for Social Policy and Management, Brandeis University, Waltham, MA, USA (E Dunham)

Correspondence to: Dr Sari L Reisner, Division of General Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA sari.reisner@childrens.harvard.edu

Panel 1: Definitions: transgender people and gender minorities

Transgender people have a current gender identity or expression that is different from the sex assigned to them at birth. The term gender minority was introduced in 2011 as part of the landmark Institute of Medicine report commissioned by the US National Institutes of Health (NIH) entitled *The Health of Lesbian, Gay, Bisexual, and Transgender People: Building a Foundation for Better Understanding.*[1] Gender minority is meant to be an inclusive umbrella term which includes people who identify as transgender or have other genders. Transgender people have diverse sexual orientation identities, attractions, and behaviours.

Panel 2: Differentiating transgender people from people who are intersex

Intersex people, also known as people with disorders of sex development (DSD; or in the terms of the intersex community, diverse sexual development[10]), are those born with bodies that vary from both male and female bioanatomies, including differences of the chromosomes, gonads, genitals, or other secondary sex characteristics. Some intersex/DSD people consider themselves to be transgender; however, most do not. This research synthesis does not include a review of intersex/DSD research. Many primary issues in intersex/DSD health are different from those in transgender people (such as the need for infant genitoplasty and gonadectomy, ongoing care for intersex/DSD adults, iatrogenic effects of genital surgery and gonad removal).[10–15] The heterogeneity and complexity of intersex/DSD health warrants its own research synthesis, which is beyond the scope of the present paper.

Panel 3: Evolving terminologies

In public health research, transgender populations are categorised according to assigned sex at birth and gender identity. This is because some health indicators (eg, prostate health) are only applicable for people assigned a male sex at birth. The terms trans feminine refers to transgender people assigned a male sex at birth who are on the transgender spectrum—identifying as women, female, male-to-female (MTF), transgender women, trans women, and many other diverse gender minority identities across the world (such as hijra, kathoey, travestis, and waria). The term trans masculine describes transgender people assigned a female sex at birth who are on the transgender spectrum—identifying as men, male, female-to-male (FTM), transgender men, trans men, and many other diverse gender minority identities (genderqueer, stud, aggressive, Sadhin). Greater attention to non-binary genders is needed in research, including consideration of transgender people who do not identify as feminine or masculine, or who integrate both. Transgender people exist all over the world. Definitions and terminology continue to dynamically evolve to describe the population across different local, national, and global contexts.

health terms (eg, HIV, disease, illness, mental health), related concepts (eg, wellbeing), and social factors (eg, discrimination, stigma). Search databases included PubMed, Embase, OVID, PsycINFO, Web of Science, and ProQuest. The appendix includes a full list of search terms and databases used.

See Online for appendix

Inclusion criteria were: (1) any study design that included quantitative data about disease burden in transgender people of any age; (2) studies published between Jan 1, 2008, and Dec 20, 2014 (inclusive), to limit information to the current context for this population; (3) studies published in English, French, or Spanish. Primary exclusion criteria were: (1) studies published before 2008; (2) studies appearing online ahead of print; (3) qualitative studies; (4) studies focused on intersex individuals; (5) studies focused on neuroanatomy or neuropsychology; (6) clinical studies focused on gender reassignment outcomes including studies of sexual satisfaction and quality of life with surgical outcomes, in view of recent reviews on these topics;[8,9] (7) studies in which lesbian, gay, bisexual, or transgender (LGBT) participants or men who have sex with men (MSM) were not disaggregated by gender identity (unless data were analysed separately and meaningful inferences could be made about transgender people). Because the overall objective was to obtain epidemiological data about transgender people, sources were not excluded on the basis of quality provided that they met all the inclusion criteria and exclusion criteria (panel 2).

First and second reviewers (RM and CEH) did parallel screening of titles found in the search. If one or both reviewers selected the abstract, the full article was reviewed. If at the full article review there was a disagreement between the first two reviewers about data extraction, a third reviewer (SLR) resolved the disagreement.

We created and refined a codebook to guide data abstraction using a collaborative consensus-based process among the authors. Health-related outcome categories were identified and used to synthesise and further organise the literature reviewed. The team incorporated principles from grounded theory,[16] whereby codes were iteratively grouped into concepts and concepts into categories. Six health-related outcome categories emerged. Through this process it became apparent that stigma and discrimination were not only determinants of health (illness), but also important outcomes themselves, for transgender populations globally.

We also conducted an expert consultation with selected transgender health researchers, and additional articles that were recommended and that satisfied the inclusion criteria were included for data abstraction. We captured the number of unique studies, as well as the number of datapoints—for example, if an article reported four health

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
North America								
Bauer, 2013[17]	Ontario, Canada	Respondent-driven sampling	Trans gay, bisexual, or have sex with men	Female	173	Prevalence	None	Depressive symptoms
Moody, 2013[18]	Canada	Internet based	Transgender	Both	133	Beta	Perceived support from family, emotional stability, child-related concerns	Suicidal behaviour
Alvarez-Wyssmann, 2013[19]	Mexico City, Mexico	Chart review	HIV infected transgender men on HAART	Female	127	Prevalence	None	Diabetes
Reisner, 2014[20]	Boston, USA	Chart review	Female-to-male transgender with diagnosis of GID	Female	23	Prevalence	None	HIV seroprevalence, history of STIs, axis 1 diagnosis, axis 2 diagnosis, depression, anxiety, substance use disorder, PTSD, bipolar disorder, adjustment disorder, suicide attempt
Shipherd, 2012[21]	Boston, USA	Trans conference based	Male-to-female transsexual and cross dresser veterans	Male	43	Prevalence	None	High cholesterol, blood pressure, vision problems, hearing problems, chronic pain, arthritis, digestive problems, cancer, lung problems, kidney problems, diabetes, depression, PTSD, anxiety, other mental health
Dowshen, 2011[22]	Chicago, USA	Convenience sample	Young transgender women	Male	92	Prevalence	None	Drunk or buzzed (used drugs) in past 3 months
Garofalo, 2012[23]	Chicago, USA	Active recruitment at local transgender gathering spots and passive recruitment through flyer distribution	Young transgender women	Male	51	Prevalence	None	HIV self-report, new STI diagnosis in past 3 months
Fletcher, 2014[24]	Los Angeles, USA	Venue-based recruitment	Community-based HIV prevention programme attendees	Male	517	Prevalence	Marginally homeless, homeless	HIV self-report, cocaine use in past 30 days, crack use in past 30 days, methamphetamine use in past 30 days, heroin use in past 30 days, marijuana use in past 30 days, hormone use in past 30 days
Reback, 2014[25]	Los Angeles, USA	Outreach based	Male-to-female transgender	Male	2136	Adjusted odds ratio; prevalence	African-American, methamphetamine, crack, injection drug, sex work, unprotected anal sex with sex work partner	HIV self-report; alcohol in past 30 days, marijuana in past 30 days, cocaine in past 30 days, crack in past 30 days, injection of drug or hormone
Simons, 2012[26]	Los Angeles, USA	Clinic-based recruitment	Transgender adolescents	Both	28	Prevalence; Pearson's correlation coefficient	Less parental support	Substantial depression; higher rates of depression
Simons, 2013[27]	Los Angeles, USA	Clinic-based recruitment	Transgender young people	Both	66	Beta	Parental support	Depressive symptoms
Rohde Bowers, 2011[28]	Los Angeles County, USA	Venue based	High risk HIV prevention programme attendees	Male	1033 (320 transgender)	Prevalence	None	HIV self-report, alcohol (five or more drinks), marijuana, methamphetamine, injected methamphetamine, cocaine, crack, ecstasy, GHB, amyl nitrate, heroin, injected heroin, hormones (non-prescribed), injected hormones

(Table 1 continues on next page)

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Benotsch, 2013[29]	Mid-Atlantic, USA	Clinic-based recruitment	Transgender	Both	155	Prevalence	Individuals reporting non-medical use of prescription drugs	HIV self-report, BSI-depression, BSI-anxiety, BSI-somatic distress, BSI-Global Severity Index, alcohol use in past 3 months, cocaine use in past 3 months, methamphetamine use in past 3 months, marijuana use in past 3 months, poppers in use past 3 months, ecstasy use in past 3 months, heroin use in past 3 months, other recreational drug use in past 3 months
McElory, 2012[30]	Missouri, USA	Pride festivals recruitment	Sexual and gender minority individuals	NS	6537	Prevalence	None	Smoking
Irwin, 2014[31]	Nebraska, USA	Community and internet based	LGBT adults	Both	770 (92 transgender)	Adjusted odds ratio	Transgender	Suicidal ideation
Reisner, 2010[32]	New England, USA	Venue based	Transmen	Female	16	Prevalence	None	Herpes self-report, trichomonas self-report, bacterial vaginosis self-report, alcohol use during sex, marijuana use during sex, hallucinogen use during sex, ecstasy use during sex
Shipherd, 2011[33]	New England, USA	Trans conference	Transgender	Male	97	Prevalence	None	Post-traumatic stress disorder, depressive symptoms
Hwahng, 2014[34]	New York, USA	Organisation based, venue referrals, and internet	HIV uninfected male-to-female transgender	Male	572	Prevalence	None	Major depression (early and late adolescence), suicidal ideation (early and late adolescence)
Koken, 2009[35]	New York, USA	Peer outreach and snowball	Transwomen	Male	20	Prevalence	None	HIV self-report
Leinung, 2013[36]	New York, USA	Clinic-based recruitment	Transsexual	Male	192	Prevalence	None	Drug and substance use, HIV
				Female	50	Prevalence	None	Drug and substance abuse
Nuttbrock, 2009[37]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	571	Odds ratio	Commercial sex partners, androphilic, unemployment, sex identity disclosure, female attire in public, casual sex partners, substance use, psychoactive drug injection, Hispanic	HIV infected, syphilis, hepatitis B, hepatitis C
Nuttbrock, 2010[38]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	571	Prevalence	None	Lifetime major depression, lifetime suicide plans, lifetime suicide attempt
Nuttbrock, 2013[39]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	230	Adjusted odds ratio; odds ratio	Employment, sex work, transgender presentation, hormone therapy; psychological gender abuse, physical gender abuse	Major depression

(Table 1 continues on next page)

outcomes, it contributed four datapoints to the review. Similarly, if data were reported for specific subgroups (eg, mental health prevalence estimates for trans feminine and trans masculine people separately), these were counted as unique datapoints and extracted accordingly (panel 3).

Overall research trends

We identified 116 studies in 30 countries. Table 1 presents the health outcome studies and key data extracted from each study by region, country, and author. Table 2 presents health-related data on stigma, discrimination, violence and

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Nuttbrock, 2013[40]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	230	Prevalence; hazard ratio	Gender abuse, education, preoperative, non-white ethnicity, committed partners (unprotected) receptive anal intercourse, commercial partners (unprotected) receptive anal intercourse, depressive symptoms, legitimate income, hormone therapy, sexual reassignment surgery, younger age, sexually attracted to men only, casual partners (unprotected) receptive anal intercourse, CES-D score ≥20	HIV seroprevalence, depression; incident HIV/STI, depressive symptoms
Nuttbrock, 2014[41]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	230	Adjusted odds ratio	Income, sex work, transgender presentation, hormone therapy, gender abuse, depressive symptoms	Alcohol use, cannabis use, cocaine use, any substance use
Pathela, 2014[42]	New York City, USA	HIV/STD surveillance registries	Transgender women living with HIV	Male	345	Incidence	Transgender, diagnosed with HIV at a younger age, living with HIV for less time	STD co-infection with HIV
Flentje, 2014[43]	San Francisco, USA	Clinic-based recruitment	Individuals entering substance abuse treatment	Male	13649 (146 transgender)	Prevalence; adjusted odds ratio	Transgender status	Methamphetamine; alcohol, cocaine, heroin, marijuana, other drug use
				Female	13649 (53 transgender)	Prevalence	None	Alcohol, cocaine, heroin, methamphetamine, other drug use
Gamarel, 2014[44]	San Francisco, USA	Purposive sampling in community spaces	Transgender females and their primary non-transgender male partner	Male	382 (191 transwomen)	Adjusted odds ratio	Financial hardship, discrimination, relationship stigma	Depressive distress
Jefferson, 2013[45]	San Francisco, USA	NS	Transwomen	Male	100	Adjusted odds ratio; odds ratio	Coping self-efficacy; transgender identity, racism, transphobia, high combined discrimination	Depression
Operario, 2011[46]	San Francisco, USA	Venue based	Transgender adults in relationship with non-trans men	Male	174	Prevalence	None	HIV self-report, STI diagnosis or symptoms past 12 months, any alcohol use in past 3 months, any illicit drug use in past 3 months, any injection drug use in past 3 months, depression
Operario, 2014[47]	San Francisco, USA	Purposive community sampling	Self-identifying transgender women	Male	191	Prevalence	None	Self-reported HIV, depressive symptoms, alcohol intoxication in past 30 days, illicit drug use in past 30 days

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	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Rapues, 2013[48]	San Francisco, USA	Respondent-driven sampling	Male-to-female transgender	Male	314	Prevalence (RDS weighted)	None	HIV seroprevalence, HIV self-report, hepatitis C
Reisner, 2014[49]	San Francisco, USA	Purposive sampling in community spaces	Transgender females and their primary non-transgender male partner	Male	382 (191 transwomen)	Prevalence; adjusted odds ratio	Age, financial hardship, discrimination	Depressive distress, HIV self-report; non-marijuana illicit drug use
Santos, 2014[50]	San Francisco, USA	Respondent-driven sampling	Transfemale	Male	314	Adjusted odds ratio; prevalence	Any methamphetamine	HIV seroprevalence; crack cocaine, powdered cocaine, club drugs, downers, painkiller, hallucinogens, heroin, marijuana, alcohol, binge drinking, any substance
Sevelius, 2009[51]	San Francisco, USA	Clinic and location based	Transgender	Male	153	Prevalence	None	HIV self-report, injecting drug use past year, alcohol use (five or more drinks per day) stimulant use
Wilson, 2014[52]	San Francisco, USA	Respondent-driven sampling	Transgender women	Male	235	Prevalence	None	HIV seroprevalence, injection drug use
Wilson, 2014[53]	San Francisco, USA	Respondent-driven sampling	Transgender women	Male	233	Prevalence	None	HIV seroprevalence, injected drugs
Nemoto, 2014[54]	San Francisco and Oakland, USA	Purposive community sampling	Transgender women with a history of sex work	Male	573	Prevalence	Race	Depressive symptoms, self-reported HIV, STI history in past 12 months
Brennan, 2012[55]	Chicago and Los Angeles, USA	Clinic based, venue based, and peer outreach and referral	Young transgender women	Male	151	Prevalence; point biserial correlations; adjusted odds ratio	Intimate partner violence, unprotected anal intercourse, polysubstance use; three or four syndemic index factors (low self-esteem, polysubstance use, victimisation, and intimate partner violence) *vs* none	Polysubstance use; HIV self-report
Bradford, 2013[56]	Virginia, USA	Internet and peer referral	Transgender	Both	350	Prevalence	None	HIV seroprevalence
Blosnich, 2013[57]	USA	Clinic-based recruitment	Veterans Health Association users with diagnosis of GID	NS	1326 in 2009, 1162 in 2010; 1326 in 2011	Period prevalence	None	Suicide-related event
Bockting, 2013[58]	USA	Internet based	Transgender adults	Both	1093	Adjusted odds ratio	Transwomen compared with transmen, age, education, enacted stigma, felt stigma, peer support, family support, identity pride	Depression, anxiety, somatisation, Global Severity Index
Budge, 2013[59]	USA	Internet based	Transgender adults	Male	226	Beta	Transition status, social support	Depression, anxiety
				Female	125	Beta	Transition status, social support	Depression, anxiety
Effrig, 2011[60]	USA	College campus survey	College students	NS	21686 (86 transgender or "other" gender	Prevalence	None	Attempted suicide, suicidal ideation
Feldman, 2014[61]	USA	Internet based	Transgender	Both	1229	Prevalence	None	HIV self-report
Fredriksen-Goldsen, 2014[62]	USA	Community-agency based	LGBT adults 50 years and older	NS	2201 (174 transgender)	Prevalence	None	Disability, obesity

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	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Horvath, 2014[63]	USA	Internet based	Rural and urban transgender	Male	692	Prevalence	None	HIV self-report, regular heavy alcohol use, binge alcohol use, marijuana use, non-marijuana drug use
				Female	523	Prevalence	None	HIV self-report, regular heavy alcohol use, binge alcohol use, marijuana use, non-marijuana drug use
Hotton, 2013[64]	USA	NS	Young transgender women	Male	116	Prevalence; odds ratio	Life stress	Substance use in past 3 months, alcohol use in past 3 months
House, 2011[65]	USA	Internet based	LGBT adults	Both	1126 (164 transgender)	Adjusted odds ratio	Transgender compared with male	Non-suicidal self-harm, attempted suicide
Mustanski, 2013[66]	USA	Venue based	LGBT young people	Both	237 (21 transgender)	Prevalence	None	Lifetime suicidal attempt
Peitzmeier, 2014[67]	USA	Clinic based	Clinic patients receiving Pap tests	Female	3858 (233 transgender)	Prevalence	None	HIV seroprevalence
Rath, 2013[68]	USA	Probability based	Young adults	NS	4159 (12 transgender)	Prevalence	None	Major depressive disorder, current alcohol use, cigarette use
Reisner, 2013[69]	USA	Brief intercept	Transmasculine	Female	73	Prevalence	All health outcomes compared with depression only	Lifetime clinical depression, alcohol abuse, current or former smoking, asthma, obese; avoided or delayed health care, younger age, queer or non-binary sexual orientation
Reisner, 2014[6]	USA	Convenience sample	Transfeminine gender identity	Male	3878	Prevalence; risk ratio	Jail or prison time, mistreated or victimised in jail or prison, denied health care in jail or prison	HIV self-report, daily cigarette smoker, substance use to cope, suicide attempt
Reisner[70]	USA	Clinic based	Participants from the Community Health Center Core Data Project	Both	2653 (31 transgender)	Prevalence	Transgender	Suicidal ideation, attempted suicide ever, substance abuse history, smoking, HIV self-report
Sánchez, 2009[71]	USA	Transgender event	Male-to-female transsexuals	Male	53	Beta	Transgender-related fears	Psychological distress
Sevelius, 2009[72]	USA	Snowball sampling, listservs, websites	Trans MSM	Female	45	Prevalence	None	HIV self-report, STI diagnosis ever, HPV, gonorrhoea, chlamydia, herpes, trichomoniasis, bacterial vaginosis, hepatitis C, pelvic inflammatory disease, pubic lice
South and Central America								
Toibaro, 2009[73]	Buenos Aires, Argentina	Clinic-based recruitment	Patients at a clinic	Both	4118 (105 transgender)	Prevalence	None	HIV seroprevalence, syphilis, drug use, alcohol use
Carobene, 2014[74]	Argentina	Not specified	Trans sex workers	NS	273	Prevalence	None	HIV seroprevalence, HBV seroprevlance, HCV seroprevalence
Socias, 2014[75]	Argentina	Snowball sampling and quota sampling	Transgender	Male	452	Prevalence	None	HIV self-report
Rocha, 2013[76]	Brazil	Transvestite clinic case records	Transvestites	NS	59	Prevalence	None	Alcohol use, drug use
Johnston, 2013[77]	Dominican Republic	Respondent-driven sampling	Gay, transsexual, MSM	Male	1388 (83 transsexual)	Adjusted odds ratio	Transsexual compared with MSM	HIV seroprevalence
Aguayo, 2013[78]	Paraguay	NS	Transwomen	Male	311	Prevalence	None	HIV, syphilis
Lipsitz, 2013[79]	Lima, Peru	Clinic-based recruitment	Men and transwomen	Male	2717 (332 transwomen)	Prevalence	None	HIV seroprevalence
Verre, 2014[80]	Peru	Peer outreach and snowball	MSM and transgender women	Male	5148 (714 transgender)	Prevalence	None	HIV seroprevalence, syphilis seroprevalence
Europe								
Wierckx, 2013[81]	Ghent, Belgium	Clinic-based recruitment	Transgender persons diagnosed with GID and on cross-sex hormone therapy	Male	214	Cases per 1000 people	Transwomen compared with age matched women	Myocardial infarction, transient ischaemic health attack, type 2 diabetes,

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	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
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				Female	138	Cases per 1000 people	Transmen compared with age matched men	Type 2 diabetes, cancer
Auer, 2013[82]	Munich, Germany	Clinic-based recruitment	Transsexuals with a diagnosis of GID, no hormone therapy or reassignment surgery	Female	131	Prevalence	None	Pubertal and menstrual irregularities, premature or delayed menarche, oligomenorrhoea, polymenorrhoea, amenorrhoea, adrenal hyperplasia, polycystic ovary syndrome, hypogonadism, anorexia nervosa
				Male	192	Prevalence	None	Pubertal irregularities, delayed oigarche, cryptorchidism, no pubertal voice change
Judge, 2014[83]	Dublin, Ireland	Clinic-based recruitment	Patients with suspected or confirmed GID	Male	159	Prevalence	None	Hypertension, dyslipidaemia, diabetes, depression, schizophrenia, bipolar affective disorder, self-harm or suicide attempt, asthma, Asperger's syndrome
				Female	59	Prevalence	None	Hypertension, dyslipidaemia, diabetes, depression, schizophrenia, bipolar affective disorder, self-harm or suicide attempt, asthma, Asperger's syndrome
Manieri, 2014[84]	Torino, Italy	Clinic-based recruitment	Transgender people undergoing hormone therapy	Male	56	Prevalence	None	Obesity, hypercholesterolaemia, hypertriglyceridaemia, diabetes, metabolic syndrome, HIV seroprevalence
				Female	27	Prevalence	None	Obesity, metabolic syndrome
Imbimbo, 2009[85]	Italy	Clinic-based recruitment	Male-to-female transsexuals who had undergone sexual reassignment surgery	Male	139	Prevalence	None	Contemplated suicide, attempted suicide
Asscheman, 2009[86]	Amsterdam, Netherlands	Clinic-based recruitment	Transsexuals on cross-sex hormones	Male	966	Adjusted hazard ratio; standardised mortality ratio	Male-to-female transsexual compared with age and sex adjusted general population	Cardiovascular mortality, all-cause mortality, mortality from malignant neoplasm, AIDS, external causes, illicit drug use, suicide
				Female	365	Standardised mortality ratio	Female-to-male transsexual compared with age and sex adjusted general population	Mortality from external causes, illicit drug use
de Vries, 2010[87]	Amsterdam, Netherlands	Clinic-based recruitment	Children and adolescents referred to gender identity clinic	Both	205	Incidence	None	Autism spectrum disorder
de Vries, 2011[88]	Amsterdam, Netherlands	Clinic-based recruitment	Adults and adolescents with a diagnosis of GID	Male	207 adults, 43 adolescents	Prevalence	None	Depression, schizophrenia, hysteria, hypochondria, paranoia, psychopathic deviate, hypomania, other mental health outcomes
				Female	86 adults, 40 adolescents	Prevalence	None	Depression, schizophrenia, hysteria, hypochondria, paranoia, psychopathic deviate, hypomania, other mental health outcomes
Almeida, 2014[89]	Lisbon, Portugal	Clinic-based recruitment	Sex workers	NS	151 (20 trans-gender)	Prevalence	None	HIV seroprevalence
Guzman-Parra, 2014[90]	Malaga, Spain	Clinic-based	Transsexuals	NS	379	Prevalence	None	Lifetime only cannabis use, lifetime only cocaine use, current cannabis use

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	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Hill, 2011[91]	London, UK	Clinic-based recruitment	Transgender sex workers	Both	24	Prevalence	None	HIV seroprevalence, syphilis, genital herpes, chlamydia-negative urethritis or proctitis, gonorrhoea, chlamydia, hepatitis B, any STI
Pasterski, 2014[92]	London, UK	Clinic-based recruitment	Adults with gender dysphoria or GID	Both	91	Prevalence	None	Autism spectrum disorder
Davey, 2014[93]	England	Clinic-based recruitment	Individuals diagnosed with gender dysphoria and age and gender-matched controls	Both	206 (103 transgender)	PWI mean score; SCL-90-R mean score; SF-36 v2 mean score	Gender dysphoric	PWI total score; global severity index, somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoneuroticism; mental health component summary, social functioning, role limitations due to emotional problems, mental health
Claes, 2014[94]	UK	Clinic-based recruitment	Transsexuals	Male	103	Prevalence	None	Non-suicidal self-injury
				Female	52	Prevalence	None	Non-suicidal self-injury
Turner, 2014[95]	UK	Clinic-based recruitment	People who sell sex	Male	96 (13 transgender)	Prevalence	None	Chlamydia, gonorrhoea, genital warts
Heylens, 2014[96]	Netherlands, Belgium, Germany, Norway	Clinic-based recruitment	Adults seeking gender reassignment surgery	Both	298	Prevalence	None	One or more axis 1 personality disorders, one or more axis 2 personality disorders, affective disorders, anxiety disorders, substance-related disorders, eating disorders, psychotic disorders
Central and south Asia								
Kalra, 2013[97]	Mumbai, India	Clinic-based recruitment	Hijra (individuals who do not conform to conventional notions of male or female gender)	Male	50 (49 male, 1 female)	Prevalence	None	Depressive disorder, dysthymic disorder, alcohol abuse or dependence
Arora, 2013[98]	New Delhi, India	NS	MSM and transgender women	Male	65 (24 transgender)	Prevalence	None	Anal dysplasia
Ramakrishnan, 2012[99]	Tamil Nadu, India	Probability based	Transgender	Both	807	Prevalence	None	HIV seroprevalenece, lifetime syphilis
Brahmam, 2008[100]	India	Probability based	MSM and hijra	Male	4600 (575 hijra)	Prevalence	None	HIV seroprevalence, syphilis seroprevalence, HSV-2 seroprevalence
Aghabikloo, 2012[101]	Tehran, Iran	Clinic-based recruitment	Transsexuals with GID seeking sexual reassignment surgery	Female	25	Prevalence	None	Mood disorders, anxiety disorders, suicide attempts, substance-related disorder
				Male	44	Prevalence	None	Mood disorders, anxiety disorders, suicide attempts, substance-related disorder
Ahmadzad-Asl, 2013[102]	Tehran, Iran	Chart review	Transsexuals with a diagnosis of GID	Male	138	Prevalence	None	General medical condition comorbidity; current smoker, psychiatric comorbidity
				Female	143	Prevalence	None	General medical condition comorbidity; current smoker, psychiatric comorbidity
Javaheri, 2010[103]	Tehran, Iran	Clinic-based recruitment	Transsexuals	Both	40	Prevalence	None	Thought of committing suicide, suicide attempt
Bhatta, 2014[104]	Nepal	Snowball/chain referral and venue based	Male-to-female transgender persons	Male	232	Prevalence	None	Alcohol in past 6 months, smoking in past 6 months

(Table 1 continues on next page)

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Rehan, 2011[105]	Karachi and Lahore, Pakistan	Random sample of gurus	Hijras	Male	400	Prevalence	None	Extra-inguinal lymphadenopathy, urethral discharge, anal discharge, anal warts, anal tears, genital ulcers
Emmanuel, 2013[106]	Pakistan	Peer referral	Key populations	Male	16642 (3714 hijra sex workers)	Prevalence	None	HIV seroprevalence, injected drugs in past 6 months
Southeast Asia								
Chemnasiri, 2010[107]	Bangkok, Chaing Mai, Phuket, Thailand	Venue-day-time	MSM and transgender women	Male	827 (241 transgender)	Prevalence	None	HIV seroprevalence, history of STIs, used alcohol ever, used drugs ever
Gooren, 2015[108]	Thailand	Snowball sampling	Kathoeys (transgender women)	Male	60	Prevalence	None	Unprescribed hormone use
			Toms (transgender men)	Female	60	Prevalence; *t* test	Using cross-sex hormones	Unprescribed hormone use, bodily harm, mental health
Yadegarfard, 2013[109]	Thailand	Organisation-based recruitment	Transgender	Male	190	MANOVA	Age, education, >10 sexual partners	PANSI positive, PANSI negative, depression, loneliness, HIV self-report
Lai, 2010[110]	Taiwan	Recruitment letter sent	First year college students	Male	2585 (49 gender dysphoric)	Odds ratio	Gender dysphoria compared with non-gender dysphoric	Generalised anxiety disorder, panic disorder, hypochondriasis, major depressive disorder, body dysmorphic disorder, schizoid personality, suicidal ideation, anxiety disorder, depressive disorder, other mental health disorders
				Female	2615 (176 gender dysphoric)	Odds ratio	Gender dysphoria compared with non-gender dysphoric	Generalised anxiety disorder, hypochondriasis, major depressive disorder, body dysmorphic disorder, schizoid personality, suicidal ideation, anxiety disorder, depressive disorder, other mental health disorders
Oceania								
Kelly, 2014[111]	Brisbane, Australia	Venue based	LGBT young people	NS	161 (24 transgender)	Prevalence	None	Alcohol, tobacco, any illicit drug use, poly-drug use, cannabis, stimulants, inhalants, prescription, medications, LSD, opiates, steroids
Pell, 2011[112]	Sydney, Australia	Clinic-based recruitment	Transgender	Male	141	Prevalence	None	Mental health diagnosis, HIV, past or present intravenous drug use
				Female	17	Prevalence	None	Mental health diagnosis, past or present intravenous drug use
Boza, 2014[113]	Australia	Internet based	Transgender identity	Both	243	Prevalence	None	Depressive symptoms, suicide attempt
Clark, 2014[114]	New Zealand	Randomly selected high school recruitment	Students	NS	8166 (96 transgender)	Adjusted odds ratio	Transgender compared with non-transgender	Substantial depressive symptoms, self-harmed in past 12 months, attempted suicide
Pitts, 2009[115]	Australia and New Zealand	Internet based	Trans people	Both	253	Number and types of discrimination	χ^2; prevalence	Depression; thoughts of suicide or hurting self in past 2 weeks, thoughts of feeling down, depressed or hopeless, major depressive episode
Multi-country								
Becerra-Fernandez, 2014[116]	Not specified, abstract	Not specified, abstract	Female-to-male transsexuals before cross-sex hormone therapy	Female	77	Prevalence	None	Obesity, polycystic ovary syndrome, metabolic syndrome, hyperandrogenism

(Table 1 continues on next page)

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Reisner, 2014[117]	Latin America/ Caribbean, Portugal, Spain	Internet based	MSM	Male	35483 (158 male-to-female transgender)	Prevalence	None	Suicide attempt ever, depressive distress in past week, HIV self-report, any STI in past 12 months, syphilis, gonorrhoea, chlamydia, HPV, genital herpes
				Female	35483 (32 female-to-male transgender)	Prevalence	None	Suicide attempt ever, depressive distress in past week, HIV self-report, any STI in past 12 months, gonorrhoea, HPV, genital herpes
Buchbinder, 2014[118]	Brazil, Ecuador, Peru, South Africa	NS	MSM and transgender women	Male	2499 (162 transgender women)	Prevalence, incidence	None	HIV seroprevalence
Meier, 2013[119]	19 countries	Internet-based	Female-to-male transgender	Female	503	Contrast estimate	Attracted to both men and women	Anxiety

BSI=Brief Symptom Inventory. CES-D=Center for Epidemiologic Studies Depression Scale. GHB=gamma-hydroxybutyric acid. GID=gender identity disorder. HAART=highly active antiretroviral therapy. HBV=hepatitis B virus. HCV=hepatitis C virus. HPV=human papillomavirus. HSV-2=herpes simplex virus 2. LGBT=lesbian, gay, bisexual, transgender. MANOVA=multivariate analysis of variance. MSM=men who have sex with men. NS=not specified. PANSI=Positive and Negative Suicide Ideation Inventory. PTSD=post-traumatic stress disorder. PWI=Personal Wellbeing Index. SCL-90-R=Symptom Checklist 90-Revised. SF-36 v2=Short Form (36) Health Survey, version 2. RDS=respondent-driven sampling. STI=sexually transmitted infection.

Table 1: **Research on health in transgender and other gender minority populations, 2008–14, by region, country, and author**

victimisation, and sex work. Figure 1 shows the geographic distribution of current studies in transgender health. Most of the available research was from the USA. Several countries had a single study (eg, Mexico) or between two and five studies (eg, Canada, Australia, Iran). No country except for the USA had six or more studies reporting data about transgender health. Indeed, for the majority of countries no data were available, and for many, only a single study existed. Only one study was available from sub-Saharan Africa. This gap in research is important to consider in terms of the generalisability of current health research across regions and geographical settings. We noted a growing interest in transgender health research over time, particularly in the most recent years (2013 and 2014), as shown in figure 2. We also noted a dearth of research about transgender children, adolescents, and young people, with only 15 studies in these populations.

Distribution of studies by sex and gender

The distribution of studies by natal sex (sex assigned at birth) is depicted in figure 3. The majority of studies focused on natal males. Because operationalisation of "transgender" was inconsistent, generalisation of scientific findings by gender identity was difficult. Specifically, we found 95 distinct operationalisations of "transgender" across the 116 studies. These can be summarised into two approaches to measuring transgender populations: by identity-based measures (ie, identify as transgender, FTM [female-to-male transgender], MTF [male-to-female transgender], trans masculine, trans feminine, transsexual, genderqueer; n=75 of 95, 79%) or by psychiatric clinical diagnostic criteria, such as gender identity disorder or gender dysphoria (n=20 of 95, 21%). The predominance of identity-based research is consistent with the trend toward de-pathologisation of gender diversity in transgender health research.[132]

Methodological limitations in current research

The most common study design was cross-sectional (90 of 116, 78% of studies). We noted a dearth of longitudinal data (seven of 116, 6% of studies), and identified only one randomised controlled efficacy trial[118] of an intervention to improve the health of transgender people globally; two studies[23,128] used a before-and-after-intervention design. Only three studies[68,99,100] were identified that used probability-based sampling methods (three of 116, 3%). Many studies used convenience sampling methods and deployed multiple sampling strategies simultaneously (eg, online, venue based, peer referral, and snowball sampling). Some sampling schemes were more focused—for example, clinic samples (29 of 116, 25%), exclusively internet-based samples (17 of 116, 15%), or respondent-driven samples (eight of 116, 7%). Most studies (95 of 116, 82%) were descriptive, only presented prevalence data (predominately unadjusted prevalences), and did not present any measures of association between risk factors or social determinants and health outcomes. Few studies compared transgender and non-transgender people (eg, by offering comparative data); most were within-group studies that did not allow documentation of health inequities.

Datapoints categorised by health outcome domain

Overall 981 unique health-related datapoints were identified from the 116 studies. Figure 4 presents these datapoints grouped into six health-related outcome categories by frequency: (1) mental health (eg, depression, anxiety), (2) sexual and reproductive health (eg, HIV,

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
North America								
Bauer, 2014[120]	Ontario, Canada	Respondent-driven sampling	Trans patients in emergency department	Male	195	RDS-weighted prevalence	None	Ever avoided emergency department because of trans identity, negative emergency department experience, refused or ended care, hurtful or insulting language, refused to discuss trans concerns, told not really trans, discouraged from exploring gender, provider did not know enough to provide care, belittled or ridiculed, thought gender marker on identification was a mistake, refused to examine parts of body
				Female	214	RDS-weighted prevalence`	None	Ever avoided emergency department because of trans identity, negative emergency department experience, refused or ended care, hurtful or insulting language, refused to discuss trans concerns, told not really trans, discouraged from exploring gender, provider did not know enough to provide care, belittled or ridiculed, thought gender marker on identification was a mistake, refused to examine parts of body
McGuire, 2010[121]	California, USA	Gay Straight Alliance organisation-based recruitment	LGBT and allies students	NS	2260 (68 transgender)	*t* test	Transgender compared with non-transgender	Feeling unsafe at school
Harawa, 2010[122]	Los Angeles, USA	Random sample from prison census	MSM and male-to-female transgender inmates	Male	101 (19 transgender)	Prevalence	None	Receiving money, protection, food, or other goods in exchange for sex
Rohde Bowers, 2011[28]	Los Angeles County, USA	Venue based	High risk HIV prevention programme attendees	Male	1033 (320 transgender)	Prevalence	None	Exchanged sex
Hwahng, 2014[34]	New York, USA	Organisation based, venue referrals, and internet	HIV uninfected male-to-female transgender	Male	572	Prevalence	None	Verbal gender abuse in early adolescence, physical gender abuse in early adolescence, verbal or physical gender abuse in early adolescence, verbal gender abuse in late adolescence, physical gender abuse in late adolescence, verbal or physical gender abuse in late adolescence
Nuttbrock, 2010[38]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	571	Prevalence	None	Lifetime gender-related psychological abuse, lifetime gender-related physical abuse
Nuttbrock, 2013[39]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	230	Adjusted odds ratio	Employment, sex work, transgender presentation, hormone therapy	Psychological gender abuse, physical gender abuse
Nuttbrock, 2013[40]	New York, USA	Organisation based, venue referrals, internet advertisements	HIV uninfected male-to-female transgender	Male	230	Prevalence	None	Psychological or physical gender abuse, psychological and physical gender abuse
Reisner, 2010[32]	New England, USA	Venue based	Transmen	Female	16	Prevalence	None	Sex work ever, internalised homophobia
Rapues, 2013[48]	San Francisco, USA	Respondent-driven sampling	Male-to-female transgender	Male	314	Prevalence (RDS weighted)	None	Commercial sex work

(Table 2 continues on next page)

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Sevelius, 2009[51]	San Francisco, USA	Clinic and location based	Transgender	Male	153	Prevalence	None	Sex work
Wilson, 2014[53]	San Francisco, USA	Respondent-driven sampling	Transgender women	Male	233	Prevalence	None	Engagement in sex work
Nemoto, 2014[54]	San Francisco and Oakland, USA	Purposive community sampling	Transgender women with a history of sex work	Male	573	Prevalence	Race	Sex work in past 6 months
Brennan, 2012[55]	Chicago and Los Angeles, USA	Clinic based, venue based, and peer outreach and referral	Young transgender women	Male	151	Prevalence; point biserial correlations; beta	Intimate partner violence, unprotected anal intercourse, polysubstance use; syndemic index (low self-esteem, polysubstance use, victimisation, intimate partner violence)	Victimisation, intimate partner violence; history of sex work
Bradford, 2013[56]	Virginia, USA	Internet and peer referral	Transgender	Both	350	Prevalence; adjusted odds ratio	Suburban *vs* urban setting, female-to-male spectrum, racial or ethnic minority, education, low income, living full time in current gender identity, age at transawareness, hormone therapy, hormone therapy needed but not obtained past 3 months, counselling or psychotherapy needed but not obtained in past 3 months, forced or unwanted sex, physically attacked, tobacco problem ever, drinking problem, family not supportive, being connected to the transgender community, hostility or insensitivity in school	Health-care discrimination, employment discrimination; discrimination
Benotsch, 2013[29]	Mid-Atlantic, USA	Clinic-based recruitment	Transgender	Both	155	Prevalence	Individuals reporting non-medical use of prescription drugs	Discrimination of the basis of gender identity
Bockting, 2013[58]	USA	Internet based	Transgender adults	Both	1093	Prevalence, beta	Non-white race or ethnicity, income, investment in passing, outness, age, transgender women compared with transgender men	Enacted stigma, felt stigma
Cruz, 2014[123]	USA	Internet based	Transgender participants from the National Discrimination Survey	Both	4049	Prevalence; odds ratio	Trans discrimination or both discrimination and affordability; male *vs* other identity, female *vs* male identity, female *vs* other identity, somewhat genderqueer identity, hormones, top surgery, bottom surgery, main place seeking care, no health insurance, income	Postponement of curative care because of discrimination
Dank, 2014[124]	USA	School-based recruitment	Students	NS	5647 (18 transgender)	Prevalence	Transgender status	Physical dating violence, psychological dating abuse, cyber dating abuse, sexual coercion

(Table 2 continues on next page)

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
House, 2011[65]	USA	Internet based	LGBT adults	Both	1126 (164 transgender)	Prevalence	None	Interpersonal trauma, experiences of discrimination
Kosciw, 2009[125]	USA	Internet based	Secondary school students	NS	5420 (245 transgender)	Beta	Transgender identity compared with male identity	Victimisation related to sexual orientation, victimisation related to gender expression
Mitchell, 2014[126]	USA	Internet based	13–18 year olds completing Teen Health and Technology survey	Both	5498 (189 transgender, 209 gender non-conforming or other gender)	Prevalence; adjusted conditional odds	Transgender *vs* cisgender male, gender non-conforming or other gender *vs* cisgender male	Sexual harassment (any mode, in person, online, by text message, by phone call, some other way), made obscene or sexual comments, asked for sexual information, asked to do something sexual, touched grabbed or pinched, showed or sent obscene or sexual messages, intentionally brushed up against, spread sexual rumours, blocked or cornered; non-distressing sexual harassment; distressing sexual harassment
Reisner, 2013[69]	USA	Brief intercept	Transmasculine	Female	73	Prevalence	None	Perceived discrimination by health-care provider
Reisner, 2014[5]	USA	Convenience sample	Transfeminine gender identity	Male	3878	Prevalence; risk ratio	Jail or prison time, mistreated or victimised in jail or prison, denied health care in jail or prison	Denied health care in jail, mistreated victimised in jail or prison; sex work, any physical assault, any sexual assault
Reisner, 2014[70]	USA	Clinic based	Participants from the Community Health Center Core Data Project	Both	2653 (31 transgender)	Prevalence	Transgender	Childhood abuse, experienced intimate partner violence, any victimisation as adult, verbally attacked, physically attacked, sexually harmed, any discrimination, employment discrimination, health-care discrimination
Ybarra, 2014[127]	USA	Targeted online recruitment	LGBT young people	Both	5542 (442 transgender)	Prevalence	None	Online peer victimisation: bullying, in-person peer victimisation: bullying, online peer victimisation: sexual harassment, in-person peer victimisation: harassment
South and Central America								
Marin, 2013[128]	Argentina	Sexual Workers Union registration	Female sex workers and transvestites	NS	950 (110 transgender)	Prevalence	None	Discrimination in health care
Socias, 2014[75]	Argentina	Snowball sampling and quota sampling	Transgender	Male	452	Prevalence; χ^2; adjusted odds ratio	Any internalised stigma, history of sex work, experienced police violence, ever arrested, perceived discrimination by health-care workers, perceived discrimination by patients, current residency in Buenos Aires; extended health insurance	Sex work, health-care avoidance because of transgender identity

(Table 2 continues on next page)

STIs), (3) substance use (eg, alcohol, drugs), (4) violence and victimisation (eg, sexual and physical abuse), (5) stigma and discrimination (eg, internalised stigma, termination of employment), and (6) general health (eg, diabetes, cancer). The available data show that transgender populations worldwide face a high burden of adverse health and disease outcomes. We briefly summarise data for each health outcome category.

Mental health

Mental health is the most commonly studied area of transgender health (n=303 datapoints; 31%). The majority of data focuses on mood disorders (n=96, 32%), suicidal and non-suicidal self-injury (n=50, 17%), and anxiety disorders (n=44, 15%). Mental health outcomes were inconsistently operationalised across studies. For example, within mood disorders (n=96), we identified 80 datapoints

	Location	Sampling method	Sample	Assigned sex at birth	Sample size	Measure of prevalence or association	Significant associations	Health outcome measures
(Continued from previous page)								
Delgado, 2014[129]	Chile	Snowball	Gay men and transgender women	Male	437 (121 transgender)	Prevalence	None	Not being hired or being fired, being denied access or permanence in a public place, poorly assisted by public officials, not accepted or excluded from school, not accepted or excluded from a group of friends, molested or harassed by neighbours, not accepted or excluded from a social group, not accepted or excluded from family, not accepted or excluded from a religious environment, verbal or physical mistreatment or being denied help by the police
Miller, 2011[130]	Guatemala City, Guatemala	Respondent-driven sampling	MSM and transgender women	Male	505 (99 transgender)	Prevalence	None	Transactional sex
Europe								
Prunas, 2014[131]	Milan, Italy	Census	Transgender victims of transphobic murder	Male	20	Prevalence	None	Sex work, primary indicator of LGBT hate crime, secondary indicator of LGBT hate crime
Central and south Asia								
Brahmam, 2008[100]	India	Probability based	MSM and hijra	Male	4600 (575 hija)	Prevalence	None	Selling sex
Javaheri, 2010[103]	Tehran, Iran	Clinic-based recruitment	Transsexuals	Both	40	Prevalence	None	Being discriminated against for being transsexual
Oceania								
Pell, 2011[112]	Sydney, Australia	Clinic-based recruitment	Transgender	Male	141	Prevalence	None	Past or present sex work
Multi-country								
Reisner, 2014[117]	Latin America/ Caribbean, Portugal, Spain	Internet based	MSM	Male	35483 (158 male-to-female transgender)	Prevalence	None	Transactional sex in past 12 months, childhood gender-related harassment, adulthood gender-related harassment
				Female	35483 (32 female-to-male transgender)	Prevalence	None	Transactional sex in past 12 months, childhood gender-related harassment, adulthood gender-related harassment

LGBT=lesbian, gay, bisexual, transgender. MSM=men who have sex with men. NS=not specified. RDS=respondent driven sampling.

Table 2: **Research on health and stigma, discrimination, violence or victimisation, and sex work in transgender and other gender minority populations, 2008–14, by region, country, and author**

focused on depression. Many studies of depression used diverse clinical screening cutoffs for clinical syndromes (eg, depressive distress in the past week, assessed by Center for Epidemiologic Studies Depression Scale [CESD] with differing cutoffs), differing timeframes of assessment (eg, lifetime depression, depressive distress in the past week, clinical diagnosis of current major depressive episode), and heterogeneous subpopulations of transgender people (eg, MTF, hijra, FTM). Despite these limitations, data consistently showed that transgender adults are burdened by mental health concerns. For example, estimates of depression prevalence were as high as 64% (CESD 16 or higher) in a sample of 573 transgender women[54] and 63% (CESD 20 or higher) in a sample of 230 male-to-female transgender people.[40] Studies using a clinical diagnosis of depression show lower prevalences than those using screening tools. For example, 31% of 207 MTF individuals were in the clinical range of the Minnesota Multiphasic Personality Inventory in Amsterdam[88] and 36% of 253 transgender people had a current major depressive episode in an Australian study.[115]

Understanding risk factors for mental health problems is crucial to decreasing global mental health morbidity, yet remarkably few studies have contributed to such an understanding in transgender people. The majority of mental health research (n=161 of 303 datapoints, 53%) reported prevalence data only. Measures of association between risk factors and mental health conditions are an important area for future research efforts. Additional gaps in mental health research included a scarcity of studies examining post-traumatic stress disorder or traumatic stress (n=3 datapoints), which is surprising,

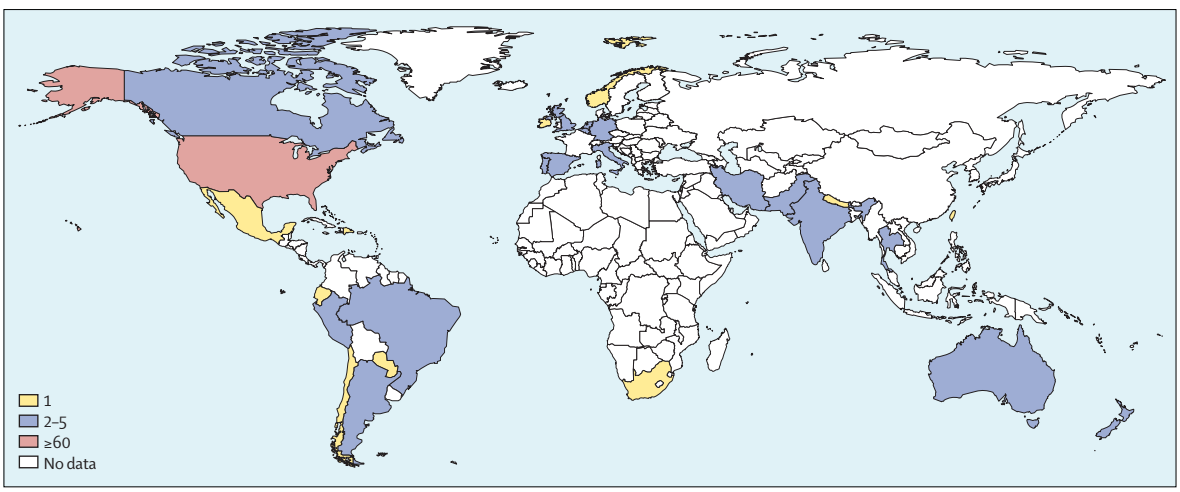

Figure 1: **Distribution of 116 studies about transgender health**

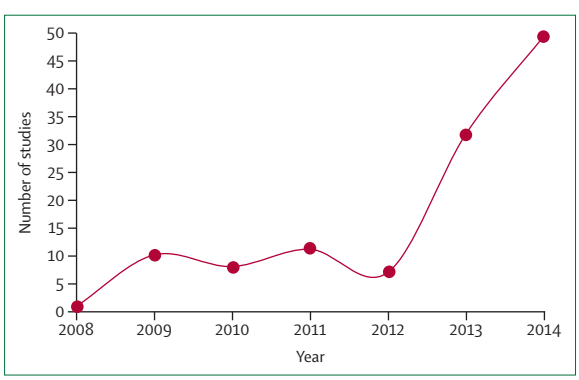

Figure 2: **Number of studies about transgender health published per year**

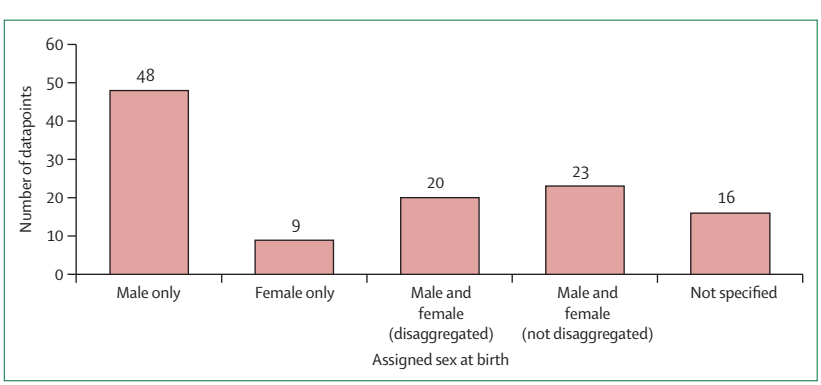

Figure 3: **Distribution of 116 studies about transgender health by assigned sex at birth**

since many transgender people experience violence and victimisation; and there were few data about eating disorders (n=3 datapoints), despite the body image concerns of transgender people[133] and the hypothesised relation between body image and sexual risk.[134]

Sexual and reproductive health

Sexual and reproductive health was the second most frequently studied area of transgender health (n=219 of 981 datapoints; 22%). The number of datapoints related to sexually transmitted infections (STIs) compared with those for other sexual and reproductive health outcomes is inflated because many studies of STIs tested for several specific organisms (eg, gonorrhoea and chlamydia), thereby creating multiple datapoints. Transgender women are disproportionately affected by HIV and other STIs, so it may not be surprising that 75% (163 of 219) of the sexual and reproductive health outcomes reported include HIV or STI prevalence. However, when the data are examined by assigned sex at birth, it becomes clear that this focus on HIV and STIs reflects a focus on transgender people assigned a male sex at birth. The findings also show that other sexual and reproductive health concerns receive little attention in research among transgender populations. For example, only 15 datapoints addressed non-infectious reproductive health concerns, and none addressed fertility or pregnancy.

Substance use

Substance use was the third most frequently studied health indicator (n=193 of 981 datapoints). Data most commonly focused on alcohol (n=35 datapoints, 18%), marijuana (n=25 datapoints, 13%), any illicit drug use (type not specified, n=16 datapoints, 8%), and tobacco use (n=14 datapoints, 7%). A noteworthy finding was that research on substance abuse, dependence, or disorder only comprised 5% of substance use data (n=10 datapoints). Substance use outcomes were heterogeneous and inconsistently operationalised across datapoints, including time of recall (eg, last 30 days, last 3 months, past 6 months, last year, lifetime), which made comparison across studies difficult. Substance use has been conceptualised as a coping mechanism to manage minority stress;[135] however, data examining this association among transgender people are scarce.

Violence and victimisation

Research on experiences of violence, victimisation, or both among transgender people faces methodological challenges, most commonly the use of unstandardised and often non-validated measures of violence and victimisation. Despite these limitations, research shows a high burden of violence and victimisation experiences in transgender people globally. Overall, 105 datapoints were identified examining violence or victimisation in transgender people, of which 80 datapoints (76%) presented prevalence data only. The median prevalence estimate for experience of violence or victimisation was 44%. Types of violence or victimisation datapoints were sexual (34%), physical (17%), psychological or emotional (7%), verbal (4%), or type not specified (38%). Verbal and psychological or emotional violence and victimisation appear to be under-researched, which highlights the need for studies to include multiple dimensions of abuse.

Stigma and discrimination

Only 14 articles (93 datapoints) in the published literature included stigma or discrimination as health outcomes. Of these 14 studies, the majority (n=10) were conducted in North America. Chile, Argentina, and Iran were the only other countries that published data on stigma or discrimination against transgender people as health outcomes, leaving notable gaps in data from regions outside North and South America. A little over half (54%) of outcomes specifically addressed stigma and discrimination in health care, including the occurrence of denial of care and postponement of care due to stigma. However, there remains a dearth of literature on the outcomes of interventions designed to reduce anti-transgender stigma and discrimination. Clearly, more research is needed to better understand how to address stigma and discrimination to improve health-care access and use for transgender populations (panel 4).

General health

The general health of transgender people is the least researched aspect of the transgender global burden of disease. The general health category—which included outcomes such as mortality, diabetes, hormone use, metabolic syndrome, and cancer—had the fewest datapoints (n=68 of 981 datapoints), with 40 distinct health indicators, 28 of which had only a single data point. The majority of research (77%, n=52) reported unadjusted prevalence estimates only.

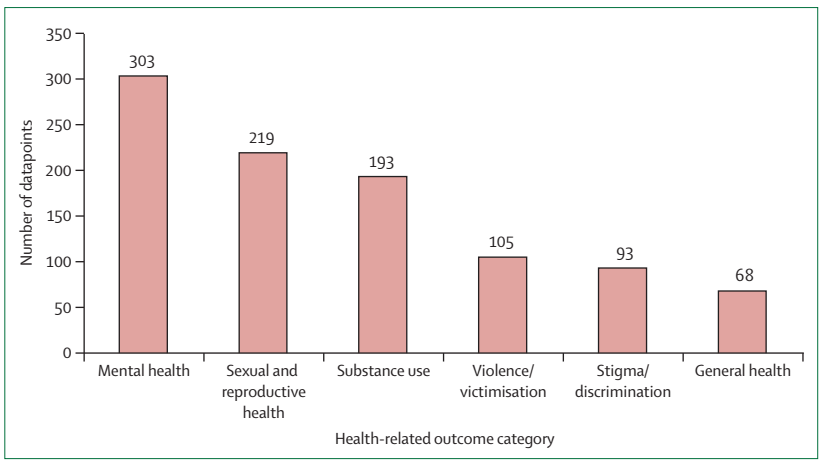

Figure 4: **Distribution of 981 datapoints from research about transgender health, grouped by six health-related outcome categories**

Panel 4: Gender affirmation: a key determinant of transgender health

A key social determinant of health for transgender populations worldwide is gender affirmation, which has been defined as an interpersonal and shared process through which a person's gender identity is socially recognised.[136–138] However, gender affirmation is not only social—social recognition of gender also involves other institutions, such as health care and law. Gender affirmation can thus be conceptualised as having four core facets: social (eg, name, pronoun), psychological (eg, internal, felt self), medical (eg, cross-sex hormones, surgical intervention, other body modification), and legal (eg, legal gender markers, name change). Gender affirmation depends on a range of factors—including context and setting (country and region) and issues relating to accessibility of cross-sex hormones (in terms of availability of medications, accessibility to culturally competent health-care providers), socioeconomics and poverty, criminalisation of sexual and gender minorities, legal barriers to changing gender markers and identity recognition, and so on. There is no single path to gender affirmation—no single approach describes how transgender people affirm and embody their gender.[139] Some people may socially, but not medically, affirm their gender; others may socially and medically but not legally do so. Gender affirmation sometimes, but not always, conforms to binary categories of being female or male. Non-binary refers to having a transgender identity that does not use female or male dichotomies as reference points.

Current gaps and opportunities

For transgender people, health inequities are hypothesised to arise from systematic exposure to multiple, intersecting social stressors, including legal and other structural factors that are a result of being part of a socially marginalised group.[140] Social and economic exclusion are therefore conceptualised as causal pathways to adverse health—however, we found very few studies actually linking these social stressors to health indicators. Furthermore, study designs were largely cross-sectional, which limited the ability to make causal inferences. Also scarce were intervention studies examining changes in health status alongside implementation of heath behaviour or other social and structural change interventions to improve the lives of transgender people. Studies of legal issues and their effect on transgender health are needed, including research on structural factors relating to human rights, such as criminalisation (related to gender identity and expression as well as sex work) and legal recognition.

The way forward: recommendations

We now offer recommendations based on our research synthesis to guide future health research focused on transgender populations.

Panel 5: **The right to inclusion in health surveillance**

A first-line argument made for non-inclusion of measures to identify transgender people in routine health surveillance efforts has been the small population size. How large is the transgender population globally? It depends how the population is measured. Over the past 15 or so years there has been a paradigm shift in transgender health from a disease-based model (transgender as disorder or mental health diagnosis) to an identity-based model (transgender as identity).[4,132,139] Conceptualising transgender people as having diverse, non-pathological genders rather than as disordered redefines how a case is operationalised and measured in health research.[145] Such redefinition of a case also necessarily affects prevalence estimates as to the number of transgender people in the world and, potentially, estimation of the distribution, burden, and magnitude of disease inequity in the population. Still, most conservative estimates suggest that 0·1–0·5% of the world's population might be transgender.[146,147] Assuming that the world's population is approximately 7 billion people,[148] the global population of transgender people might be estimated at 7 million to 35 million. That said, does the number of transgender people matter more than the fact that the population is so grossly underserved worldwide?

Count transgender populations

Social determinants, such as age, sex, gender, race, and socioeconomic status, shape the health status of people across the world. WHO defines social determinants of health as "the conditions in which people are born, grow, live, work and age" and states explicitly that "these circumstances are shaped by the distribution of money, power and resources at global, national and local levels".[141] Social inequalities resulting from social determinants are conceptualised as driving health inequities.[142] Health inequities refer to avoidable, remediable, unfair health inequalities between populations.[142] A social determinants perspective explicitly links reductions in health inequality to achievement of health equity.[143]

Health inequality monitoring refers to the systematic tracking of health inequalities over time, including measures of the magnitude of disparities in the face of interventions such as policies, programmes, and practices.[144] Equity stratifiers refer to the dimensions of social inequalities being monitored (such as place of residence, or race or ethnicity).[144] Few population level data exist with which to monitor the health of transgender people worldwide, because routine national and international health surveillance efforts in most countries do not assess gender identity as an equity stratifier. This omission creates a major gap in the ability to further understand the health inequities burdening transgender people (panel 5). It is also a missed opportunity to understand the relation between intersecting social statuses (such as disability status and caste) and health. There is a need for surveillance definitions of transgender people for global use. Studies restricting samples to people with diagnosed gender identity disorder or gender dysphoria do not capture the range of transgender people who comprise the overall population, such as those with non-binary transgender identities.

As Winter and colleagues described in paper 1 of this Series,[4] a two-step method is recommended to capture health-related data by transgender status.[3,117,149,150] This method uses assigned sex at birth and current gender identity to cross-classify respondents as transgender (discordant sex and gender responses) or non-transgender (concordant sex and gender responses). It also allows diverse gender identities to be captured. Researchers have operationalised the two-step method using a range of question and response options (panel 6). Methods have also differed as to the order of question asking (sex followed by gender identity, or vice versa) and whether respondents are asked to select one gender identity option or are allowed to select multiple options. The strength of a two-step method is that it explicitly captures dimensions of both natal sex and current gender identity. It also permits categorisation of subpopulations of transgender people by natal sex and gender identity. A two-step method has not been used widely across the world. Studies are needed that implement this approach in different contexts and settings using consistent definitions of transgender. We recommend that special care be taken in designing instructions and introductory text for the two-step method, including adaptations for the specific geographical context in terms of language and cultural understandings of sex and gender. Training of interviewer staff and research teams is also recommended, as well as a process to confirm transgender responses in order to minimise misclassification bias.

Put the gender back into transgender health

Sex and gender are determinants of health across a wide variety of geographical contexts.[141,159–164] Causal mechanisms for poor health are related to both sex and gender; however, sex and gender are commonly conflated in research.[159] For example, terms referring to assigned sex at birth ("male" and "female") and gender identity ("men" and "women") are commonly used interchangeably in the scientific literature, including in transgender research. This practice leads to a lack of attention as to whether health differences are due to sex, gender, both, or neither,[159] which affects understanding of health inequities. Synthesis of research on the health of transgender people reveals gaps in the specificity and operationalisation of sex and gender differences in population research more broadly.

Development of new conceptual models and integration and testing of existing frameworks is needed to guide research in transgender population health. Several conceptual models have been applied to transgender health, including social determinants and social ecological models,[141,165] gender affirmation,[136] gender minority stress,[58,135,166] syndemic production,[167] and health and human rights approaches.[2,168] These models overlap in their shared recognition that multiple and intersecting levels of risk and resiliency shape the health of transgender people and that, therefore, multilevel contextually relevant interventions are necessary. However, these models do not apply a gender analysis,[159] a

social epidemiological approach that explicitly considers socially derived gender exposures and outcomes, sex-linked physiological or biological differences, and the interplay of both gender and sex.[158,159,169,170] Transgender people share many of the same risks and social and structural determinants of disease, health, and wellbeing as non-transgender people (such as socioeconomic status). However, transgender people also experience unique biological, behavioural, social, and structural contextual factors surrounding health risks and resiliencies—including those related to challenging the congruence or conflation of sex and gender such as legal recognition of gender identity. We therefore recommend that future research in transgender population health use a gendered situated vulnerabilities framework to investigate whether and how sex-gender mechanisms[159] shape health-related risks and resiliencies for population health outcomes.

Gendered situated vulnerabilities refer to the ways in which health is shaped by the distribution of power along lines of gender.[171,172] The vulnerabilities transgender people face regarding health are related to challenging gendered relations of power and policing of gender by social structures. We refer to these as situated because the health risks and resiliencies facing transgender populations cannot be understood without the multilevel sexed and gendered contexts that shape them. We use the term vulnerabilities to describe the ways that these contexts put transgender people "at risk for risk".[173,174] We do not conceptualise transgender people as an inherently vulnerable population; but rather, view this community as a population facing sex and gender related situated vulnerabilities for different health conditions. As shown in the synthesis of current research, some of the health conditions differentially distributed by transgender status include mental health, infectious diseases, and substance use and abuse.

Integrate health and human rights and multi-sectorial approaches

Transgender people have the right to legal recognition of their gender identity, access to gender affirmation, and a right to self-determination and autonomy.[175–178] Although the Office of the UN High Commissioner for Human Rights denounces widespread discrimination against transgender people,[7] systematic social and economic marginalisation, stigma, pathologisation, discrimination, violence, and other human rights violations, including those in health care, continue to drive or exacerbate health inequities. To improve the health and access to health care of transgender people globally requires a wide array of stakeholders and mobilisation of diverse multi-sector partnerships. Many barriers to health care and adverse health risks are addressable through law and policy, and some countries have begun to do so through gender identity laws, legislation about gender-affirmative care, and anti-discrimination and protective measures.

***Panel 6:* Example of two-step method in data collection**

Standardisation of data collection to routinely monitor health and disease distribution among transgender people represents a crucial step towards improving their health. A two-step method is recommended[117,151–153] by organisations including the World Professional Association for Transgender Health (WPATH).[154] Appropriate adaptations to the two-step method are needed in different geographical regions, cultures, and languages.

Reisner and colleagues[155] in 2014 implemented the two-step method in the Growing Up Today Study (GUTS), a US prospective cohort of more than 16 000 young people enrolled in 1996. Step 1 asked: "What sex were you assigned at birth, on your original birth certificate? (check one)" with response options "female" and "male". Step 2 asked: "How do you describe yourself? (check one)" with response options "female", "male", "transgender", "do not identify as female, male, or transgender". Cross-tabulation of these questions gives a two by four contingency table with eight cells showing different sex and gender combinations (table 3). Overall, 0·33% of the cohort self-identified as transgender or another gender minority in 2010.

The two-step approach can not only help to understand population size and health inequities facing transgender people, but can also aid in explicit consideration of sex and gender differences more broadly—and health inequities that may be due to assigned sex, current gender, both, or neither. The two-step method thus facilitates a gender analysis in population health.[156–158]

	Assigned sex at birth	
	Male	Female
Current gender identity		
Male	Cisgender	Trans masculine*
Female	Trans feminine*	Cisgender
Transgender	Trans feminine*	Trans masculine*
Do not identify as male, female, or transgender	Trans feminine*	Trans masculine*

Cisgender=non-transgender. *Inclusion of these cells allows overall prevalence of transgender people to be captured.

***Table 3:* Example of two-step method used to capture data about transgender people in the US Growing Up Today Study (GUTS)**

For example, in 2012, the Argentinian Senate passed the first gender identity law in the world, which authorises transgender people to change their legal gender markers through a simple administrative process, with improved access to hormonal treatments or surgical procedures (with the only requirement being informed consent, in accord with the standards of care endorsed by the World Professional Association for Transgender Health),[179,180] and under governmental coverage.[181] Evaluation of the effect of these legal changes and improvements on the health of transgender people is needed. Implementation science, an emerging domain of methods aiming to harness generalisable information that can inform the effectiveness of programmes and policies,[182] is well suited for such evaluations.

Transgender health research is not without challenges. Public health researchers must work together with policy makers, health-care providers, and communities and

their political organisations to address systematic institutionalised marginalisation. In general, social, ethnic, and psychological aspects of research are not judged to be high on the hierarchy of evidence-for-practice.[183,184] This problem is compounded by the challenges of researching a discriminated population in view of institutionalised censure, and in some cases criminalisation, of not only transgender communities themselves, but also the researchers and clinicians who engage with them. In most countries, transgender issues are not included in formal training curricula for medicine, epidemiology, public health, education, legal, and social service systems, shaping a poor foundation for research and core competency in transgender health. Integration of public health practice, research, education, advocacy, and funding is critical to address the health needs of transgender people and their allies seeking to understand and ameliorate transgender health disparities.

Engage transgender people: a participatory population perspective

Within transgender communities, immediate survival needs may supersede perceived health risks and undermine traditional research approaches—research may seem to have little meaning and relevance to people's lives. Poverty, food insecurity, mobility, and security issues might affect research participation and attrition rates, as might intersectional issues of sex work, refugee status, and homelessness. Inclusion of transgender people in public health efforts and working with the local community and its political organisations in each geographical area to advance transgender health and human rights agendas is essential. The use of a "participatory population perspective"[185] and community-based participatory research principles[186] represents an important future step to ensure that health-related research and interventions are responsive to the real-life issues that transgender people face. This means conducting research "with" and not "on" transgender populations,[187] as well as being transparent in methodological sections of research articles about whether and how transgender communities were engaged in the research process. Meaningful engagement of transgender people will ensure that research is culturally specific to local community needs, that research questions and surveys are gender affirming, and that the scientific approach (eg, study design, sampling) is appropriately aligned with and feasible for the study population.

Limitations of the review

In view of the lack of consistent definitions within research among transgender populations, a synthesis of transgender population health requires a complex set of diverse search terms and keywords to accurately identify the current health research (see appendix). Notably, the term "transgender" was only added to PubMed as a MeSH term in 2013. From 2001 to 2012, "transsexualism" was the index term. In the USA, the phrase gender minority has been used to describe transgender people, in order to include diverse gender identities, not just people who self-identify as transgender.[1] "Gender minority" is currently not indexed. We recommend that it be added as a MeSH term.

Some data characterising transgender populations did not satisfy the objectives of the review. Data describing sexual satisfaction or quality of life were not included because these measures are often reported in clinical studies of gender reassignment surgical outcomes, whereas our focus in this review was on public health studies; we refer readers to recent reviews of gender reassignment outcomes.[8,9] Studies examining neuro-anatomical or neuropsychological differences between transgender populations were excluded. These data are important, especially as new surgical procedures are developed, but they were outside of the scope of the present review.

A noteworthy limitation of this synthesis pertains to the fact that we reported data at the level of datapoints in some instances, rather than at the study level. This approach could have inflated some estimates, since studies with more datapoints contributed more data. Thus, the count of datapoints presented in this review is not to be interpreted as a measure of the quality of data. We also excluded qualitative studies, which are a rich source of inquiry.

This review was limited to peer-reviewed literature. Many non-peer reviewed sources from WHO, the Pan American Health Organization, the Public Health Agency of Canada, UNAIDS, the US Centers for Disease Control, and additional health agencies and organisations, including grassroots community-based needs assessments, provide invaluable data. Partnerships between community members and researchers to collect data represent an important step in improving transgender health research worldwide.

Conclusions

The global disease and health burden of transgender people remain understudied, particularly in relation to the effects of stigma, discrimination, social, and structural factors that affect the health of this underserved population.[48] Unavailability of standardised survey items to identify transgender respondents limits existing health surveillance efforts. Lack of consistent operationalisation of transgender status across studies limits generalisability of findings. Use of a two-step approach to standardise data collection in health—modified for the specific geographical context, language, and locale—will allow researchers, policy makers, and transgender people themselves to add to monitor and evaluate efforts to achieve health equity. Measuring sex and gender dimensions in health research will contribute to understanding and ameliorating health inequities for all.

Despite substantial gaps in empirical research, there are sufficient actionable data highlighting unique biological, behavioural, social, and structural contextual factors surrounding health risks and resiliencies for transgender people that need interventions.[48] Studies are needed that conceptually integrate and examine transgender-specific social determinants of health, including incorporating a framework of gendered situated vulnerabilities. An important next step will be a comprehensive public health approach that includes access to gender affirmation (in a social, psychological, medical, and legal context), improved health systems informed by high quality data, and effective partnerships with local transgender communities to ensure responsiveness of and cultural specificity of programming. Dedicated funding to ensure consistency of definitions for health surveillance and research initiatives involving transgender people is essential to inform evidence-based decisions about the scale and content of programmes. Multisector partnerships that integrate health and human rights are a crucial next step to advance social justice and ultimately the health of transgender people worldwide.

Contributors

SLR, TP, and SDB conceptualised the study design and wrote sections of the manuscript. SLR, TP, and SLR developed the search protocol, which was implemented by CEH, RM, and ED. All authors contributed to the writing of the manuscript. CEH, RM, and ED abstracted data, with SLR and TP acting as a tiebreaker at all stages. CEH developed the global research map.

Declaration of interests

We declare no competing interests. SLR and TP members of the World Professional Association for Transgender Health (WPATH).

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